AD NUMBER
AD818682
NEW LIMITATION CHANGE
TO Approved for public release, distribution unlimited
FROM Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; 15 DEC 1966. Other requests shall be referred to Medical Research Labs., Edgewood Arsenal, MD.
AUTHORITY
USAEA ltr, 4 Oct 1967

20 3-1

METHODS FOR MEASURING CHEMICALLY INDUCED BEHAVIORAL CHANGES IN VARIOUS MAMMALIAN SPECIES

Final Report

by

V. J. Polidora

15 December 1966

Medical Research Laboratory
RESEARCH LABORATORIES
Edgewood Arsenal, Maryland 21010
Contract DA-18-035-AMC-368(A) new

University of Wisconsin
Madison, Wisconsin 53706

Distribution Statement

This document is subject to special export controls and each transmittal to foreign governments or foreign nationals may be made only with prior approval of the Command Officer, Edgewood Arsenal, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010

Disclaimer

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

Disposition

Destroy this document when no longer needed. Do not return it to the originator.

METHODS FOR MEASURING CHEMICALLY INDUCED BEHAVIORAL CHANGES IN VARIOUS MAMMALIAN SPECIES

Final Report

by

V. J. Polidora

15 December 1966

This document is subject to special export controls and each transmittal to foreign governments or foreign nationals may be made only with prior approval of the Commanding Officer, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010.

Medical Research Laboratory
RESEARCH LABORATORIES
Edgewood Arsenal, Maryland 21010
Contract DA-18-035-AMC-368(A)
Project 1C014501B71A

UNIVERSITY OF WISCONSIN
Madison, Wisconsin 53706

(see form 1473)

FOREWORD

The work described in this report was authorized under Project 1C014501B71A, Basic Research in Life Sciences (U). The work was started in April 1965 and completed in December 1966.

In conducting the research described in this report, the investigator (or investigators) adhered to the "Guide for Laboratory Animal Facilities and Care" as promulgated by the Committee on the Guide for Animal Resources, National Academy of Sciences-National Research Council.

Acknowledgments

The continuing support, cooperation, and professional assistance generously provided by Professor Harry F. Harlow, Director of the University of Wisconsin Primate Laboratory, is gratefully acknowledged. In conducting the research reported herein, the following contributed greatly in various capacities: W. J. Thompson, W. T. Main, D. A. Losey, R. J. Urbanek, and L. A. Link.

SUMMARY

Progress during the 18-month period of this research contract is described in terms of the four principal research programs pursued: (1) Sequential responses (both monkeys and rats), (2) Vigilance, (3) Visual Exploration, and (4) Wisconsin Automatic Testing Apparatus (WATA). The most important advances in each of the programs are as follows. The monkey sequential responses research has been discontinued during the contract period because of inability to train monkeys to execute these response patterns. The rat sequential responses program has continued with the major emphasis being upon experiments on the effects of electrolytic lesions to several subcortical areas of the brain, and the effects of certain hallucinogenic agents both before and after the brain lesion. The single most important outcome of our research during the contract period has been in an outgrowth of the Vigilance program; namely, the experimental advantages of using an air-blast to motivate monkeys (and rats) in shuttle-box avoidance learning and performance. We found that an air-blast unconditioned stimulus (UCS) led to more stable and more rapid learning in squirrel and rhesus monkeys than did an electric grid shock UCS, and similar effects, including an absence of "freezing behavior," was obtained with rats. The balance of the Vigilance research was devoted to drug experiments on visual signal-from-noise detection behavior. The Visual Exploration program was devoted to determining the effects of atropine, chlorpromazine, amphetamine and chlordiazepoxide, each tested at three doses and for 10 hours. In the WATA program we have completed our experiments characterizing the stimulus correlates of visual metric pattern discriminability for learning-set sophisticated monkeys, and we have begun our next series of experiments on naive monkeys.

TABLE OF CONTENTS

1. Sequential Responses

a. Monkeys

Research on training monkeys to execute sequential response patterns within a cylindrical test chamber has proven to be singularly unsuccessful, and our efforts were terminated in the course of this research contract. Our decision to terminate this research program was based upon the negative results of a series of experiments performed during this and several previous years. Without relating each of these experiments in detail, they can be summarized as follows.

In our earliest experiments we required the monkey to touch a floor plate approximately 8 inches square in front of a given site in order to perform a response. In addition to learning that monkeys do not learn sequential response patterns under these conditions, i.e., they did not eliminate errors, we gained the impression that the animals were more willing to continuously circle the compartment and retrieve rewards when and where they were dispensed than they were willing to decrease their relatively high response rates and respond to only the correct response sites in the correct sequence. We, therefore, redesigned the animal's compartment so that the monkey was required to touch one of the reward receptacles in order to execute a response and obtain a reward. In other words, we required a more deliberate act as a response, rather than allowing a possibly "accidental" response to the floor plates to be scored as an "intentional response."

Subsequent experiments with this apparatus were not so encouraging as might have been expected. Although the monkeys learned to perform the required receptacle-touching response to obtain rewards, their response rates were very low, and they at no time showed a trend toward eliminating responses to invariably nonrewarding sites (e.g., the C-site in an A-B-D sequence), nor did it appear that they were learning the earliest stages of a given sequence (e.g., the A-B linkage of an A-B-D sequence).

Our next approach to the problem consisted of changing our subject population from mature rhesus monkeys to younger male rhesus, who have proven to be more amenable to behavioral testing in many laboratories and under a variety of different testing conditions. Once again, however, the seven naive male rhesus monkeys with which we worked for several months did not learn the required sequential response patterns--thus eliminating the subject variable as the source of our experimental difficulty.

Our final experiments in this program were designed to determine whether a tutorial approach would overcome monkeys' inability to learn sequential response patterns. Accordingly, we modified our procedure so that a light was used to illuminate the next correct response site; after a response was made to that site, then the light over the next correct site was lighted, and so on. The monkeys did learn to respond to the indicated sites, as one would expect, but after having learned to go to the correct sequence of sites, or at least to follow the light cues, the monkeys did not transfer this capacity to a no-lights condition. That is, without the cue lights they responded to the sites on a chance basis. At the completion of these experiments, we terminated further research in this program.

Although our research on this problem has been admittedly unsuccessful, the most disappointing facet of our experience is that we are even now unable to identify the source of the problem with any degree of certainty. The only reasonable interpretation of these results is that they reinforce Professor Harlow's opinion that monkeys are not rats, and that in order to behaviorally test monkeys, the experimenter should bring the problem to the monkey (as in the WGTA) rather than the converse as with rats (as in allowing the rat to traverse a maze).

b. Rats.

The sequential response program with rats has continued to be a successful one. We have completed several experiments during the contract period, with emphasis being on completing the psychological characterization of sequential response habits and on experiments on the effects of brain lesions and psychopharmacological effects.

The most important recent experiment in the former category was that in which we compared the performance of Sprague-Dawley and Holtzman strains of albino rats with the performance of the Long-Evans strain of hooded rats which we have used previously. At its inception we had planned merely to document the widely held opinion that hooded rats are far more "intelligent" than the more highly inbred, albino strains. To our complete surprise, however, the reverse proved to be the case. The two albino strains were indistinguishable, but both were superior to the hooded strain in every important respect--their response rates were higher, they learned sequential response patterns more rapidly at every level of sequence complexity, groups of albino rats performed much more comparably at any level of sequence complexity than did hooded rats (i.e., less within-group variance), and albino rats were less variable in their response to 50 or 100 microgram per kilogram doses of LSD than were hooded rats. When added to their favorable supply availability and their standardized animal care procedures and wide-spread usage in many research disciplines, these data quite strongly indicate the recommended usage of albino rat strains in psychological research. Of course the single most important reservation to this conclusion is that it probably applies only to research on nonvisual tasks such as in the sequential response situation. Various lines of evidence suggest that the hooded rat's pigmented eye is superior in acuity to the albino rat's, and for this reason alone one should expect corresponding differences in visually based discriminative behavior in these strains. But in situations involving nonvisual discriminative cues and a totally enclosed testing compartment, it would appear that albino rats are superior even on extremely complex and difficult tasks. In any event, we have incorporated these results into our program by using only an albino strain of rats (Sprague-Dawley) in our subsequent research in the sequential responses program.

Our psychophysiological experiments in this program have been primarily exploratory in nature. Using rats which had reached our standard criterion of learning--three consecutive, 20-minute sessions in excess of 90% correct site changes plus a response rate at least as great as that obtained in previous sessions--we subjected the experimental animals (controls receiving a sham operation) to electrolytic lesions to one of three areas of the brain, the head of the caudate nucleus, the septal area and the hippocampus. After recovery from surgery, each animal was retested until it reacquired asymptotic performance of its initial sequential response habit.

The results of the initial experiments showed little decrement in percentage correct site changes (CSC) and moderate but transient decrements in response rate after caudate lesions, small but transient CSC decrements and no effect on response rate after septal lesions, and relatively large and protracted (3-10 sessions) effects on CSC and no response rate after hippocampal lesions. Another important result of this experiment was that quantitatively greater deficits were obtained with animals performing sequential response habits of greater complexity. In psychophysiological as well as psychopharmacological experiments, then, the conclusion seems to hold that more complex behavior is more susceptible to experimental disruption than is more simple behavior.

Following this initial rather encouraging experiment, the lesion effects obtained being in good agreement with the existing literature, we began an extensive experiment on the effects of 200 micrograms per kilogram doses of LSD upon asymptotic sequential behavior both before, and after, the same three brain lesions. The order of treatments in each of six Sequence Complexity conditions (10 experimental and 5 sham controls in each condition) were as follows: (1) acquisition to criterion of the assigned sequential response habit; (2) saline injection immediately before one retest session of 20 minutes; (3) 200 micrograms per kilogram LSD on the following test day under similar timing and testing conditions; (4) reacquisition of the performance criterion; (5) lesion (caudate, septal, hippocampal or appropriate sham control); (6) one-week recovery; (7) reacquisition of criterion performance; (8) saline injection as before; (9) 200 μgm/kg LSD as before; (10) reacquisition of criterion performance; (11) acquisition to criterion of a more (one half of the animals) or less complex novel sequence.

The results of this experiment were more equivocal than we had expected. The predominant effect of the initial dose of LSD was a uniform and almost complete depression of response rate after about 5 minutes--for all sequences; similar but smaller effects of the second dosage were obtained after the lesion. Differential effects as a function of sequence complexity were not obtained after either administration. The effects of the brain lesions were more pronounced than were the LSD effects, and the initial effects of the three lesions were similar to those obtained in the initial experiment. Relearning of a new sequence proved to be a condition most affected by brain lesion; hippocampal rats showed severe deficits in learning a new sequence and, in fact, 55% of the animals failed to learn a new sequence within 30 additional sessions. Eighty per cent of these were animals required to learn a new sequence <u>more</u> complex than their original one. Septal rats required only a few more trials to learn a new sequence than did controls, and caudate rats were essentially unaffected. (It should be noted that the caudate-lesion group is an interesting one from the viewpoint that these rats sustain a moderate to severe deficit in motor abilities as a result of the lesion. The fact that these lesions had negligible effects upon sequential response performance is supportive evidence for the behavioral specificity of this method; that is, it is selectively more sensitive to effects on "higher order" behavior than to effects simply on sensory or motor systems.

Vigilance

Progress in our Vigilance program was materially facilitated by our work with air-blast used as an unconditioned stimulus (UCS) in shuttle-box avoidance learning. This innovation was begun early in the contract period, and

most of our efforts during the first two-thirds of the contract period were directed toward elucidating the efficacy and utility of the technique.

After some pilot research with "extra" animals, we began this program by designing an experiment around a group of 36 squirrel monkey (Saimiri sciureus) which were made available to us by another research unit of the Primate Center. (It is worth noting that these squirrel monkeys were released by the Learning research unit because of extreme and protracted difficulty in working with these animals in behavioral tasks. Unrestrained squirrel monkeys are reported to be singularly difficult to adapt and test in behavioral settings, and the experience of this research unit corroborates this report.) A complete report of this experiment has been published in the open literature (Psychonomic Science, 1967, 7, 175-176), but a few of the important features of the experiment would be of value in this report.

A conventional, small, two-compartment shuttle box (12 in. wide by 27 in. long, no hurdle) was used, with a 100 W. incandescent lamp in either end door serving as the conditioned stimulus (CS). The floor consisted of 20, 3/4 inch wide, flat, stainless steel bars running the width of the box. These bars were used both to detect the monkeys position within the box and to deliver electric grid shock when appropriate. Two 1/2-in. pipes were positioned across the width of the box one in. from, and parallel to, both the grid floor and either end of the box. The principal independent variable of the experiment was the nature of the UCS; either a 2 ma. electric grid shock or a 100 lb/in.^{2} air blast delivered through the 15, 0.043 in. holes in the appropriate air pipe.

The results of the experiment quite clearly showed that air-blast UCS led to very rapid avoidance conditioning (a median of 70 trials to a criterion of 10 consecutive avoidance responses), whereas electric shock UCS led to relative slow learning (a median of 120 trials to the same criterion) and much more variable behavior in animals under the shock conditions. A more discriminating analysis of the acquisition data, in terms of the numbers of trials each group required to attain successively more stringent runs criteria (trials to a run of one avoidance, then a run of two consecutive avoidances,..., a run of ten consecutive avoidance responses), revealed further that the air-blast groups attained these criteria at an approximately linear rate but the shock groups attained the run-of-six criterion only after 100 trials and then attained the run-of-10 criterion rapidly thereafter. These latter data show that the well-known disruptive effects of electric shock are most pronounced early in learning--having the effect of retarding the development of even moderately consistent behavior. Once a monkey had learned to avoid shock somewhat regularly, however, he seldom failed to avoid it again. Air-blast UCS apparently produced more rapid acquisition simply by not retarding it.

After this extremely encouraging result with squirrel monkeys--animals which had previously been intractable in conventional learning situations--we moved next to testing rhesus monkeys (Macaca mulatta) under similar conditions. Our first step was to build a somewhat larger test compartment to accommodate the larger monkeys, but otherwise all important details of construction were proportionally identical to the smaller compartment used with squirrel monkeys.

The first experiment employed 16 adolescent, male, rhesus monkeys in a 2 x 2 factorial design, the two variables being presence versus absence of a 6-inch barrier separating the two compartments, and nondiscriminated (no punishment for shuttling in the presnce of no CS) versus discriminated (air-blast for entering the nonsafe side in the absence of a CS) procedures with air-blast UCS only. The results showed that the hurdle had negligible effects under any conditions and that discriminated avoidance was much more difficult to learn than was nondiscriminated. On the basis of these results, we decided not to employ a hurdle and to use a nondiscriminated procedure wherever possible.

The next experiment in this program was done in collaboration with Professor Jerome S. Schwartzbaum of the Primate Center Staff. In his continuing research on the behavioral significance and neurophysiological role of the amygdaloid complex, Dr. Schwartzbaum had been planning to compare the effects of surgical ablation of this area in infant monkeys with those obtained after comparable lesions in adults. His principal difficulty in testing very young monkeys (about 1 year old after surgery and recovery) was that they were prohibitively difficult to motivate, in order to obtain stable behavioral data. At this point I suggested air-blast-motivated shuttle avoidance learning and extinction, and we agreed that it would be worth investigating, especially since we had obtained in our pilot research very good results with several 8-month-old, socially isolated monkeys.

To date eight experimental and eight sham controls have been tested when they were approximately one year of age, the experimental animals having had bilateral (two-stage) amygdalectomies performed within the first 3 months of life. The interesting finding was that both groups learned to avoid, and were extinguished, at similar rates. The rate of learning was extremely rapid in both groups--a median of 25 trials to a run-of-10 criterion--more than twice as fast as the rate obtained with adult squirrel monkeys. Other investigations have reported that monkeys amygdalectomized as adults show profound deficits in shuttle avoidance learning to electric grid shock UCS. We shall therefore produce comparable adult amygdalectomized preparations, and determine whether they show similar deficits in air-blast-motivated shuttle avoidance. If the lesioned adults show as large deficits in avoidance learning to air-blast UCS as has been obtained by others with shock UCS, the plasticity of the infant monkey brain will have been demonstrated once again--this time as related to the limbic system of the brain. If, however, the lesioned adults do not show with air-blast UCS the deficits obtained by others with shock UCS, these results will suggest that the deficits obtained with shock are peculiarly related to some reaction of the monkey to electric grid shock.

Another series of investigations which has been initiated in connection with the use of air-blast UCS was one conducted in collaboration with Dr. Robert E. Bowman of the Primate Center staff. Using Dr. Bowman's facilities, personnel and laboratory capabilities in the area of steroid biochemistry, we are determining the so-called "stress" response of monkeys--as indexed by release of 17-hydroxycorticosteroids (17-OHCS)--to several aspects of the avoidance learning situation with both shock and air-blast UCS. The goal of these experiments is to seek experimental verification of our impression that air-blasted monkeys are less "stressed" than shocked

monkeys. If this proves to be the case, the efficacy and usefulness of air-blast will be further proved and the "sufficiently aversive but noninjurious" property of air-blast will at least be indirectly proved to be a more humane, effective technique with which to study avoidance learning in animals.

Our initial results in this series of experiments are positive. The first experiments showed that most monkeys show significant elevation of plasma 17-OHCS during nontesting adaptation to the experimental chamber itself, and they subsequently habituate (lack of 17-OHCS rise) upon repeated adaptation sessions. We shall now follow the course of 17-OHCS response during learning, asymptotic performance and extinction of avoidance behavior with both air-blast and electric grid-shock UCS. Our expectation is that compared to that obtained with shock UCS, air-blast UCS will result in attenuated 17-OHCS responses during learning, more rapid habituation (smaller 17-OHCS rises which approach lack of 17-OHCS response) during repeated sessions of asymptotic performance, and more rapid extinction of behavioral as well as 17-OHCS responses under extinction conditions. These data will be obtained during the coming contract year.

The final series of experiments which grew out of our studies of air-blast-motivated shuttle avoidance learning is one in which rats are used as subjects. With an appropriately scaled down shuttle box, we have determined that air-blast UCS leads to more rapid shuttle avoidance learning even in rats. Our data on rat behavior are only fragmentary at this time, but thus far it seems quite clear that for rats air-blast is just as aversive a UCS as is electric grid shock, and, further, that it leads to rapid learning without the "freezing behavior" usually obtained when shock UCS is employed. After we have investigated the important parameters (CS-UCS interval, UCS intensity, etc.) and established normative learning and extinction rates under optimal conditions, we shall begin a series of experiments, which are of crucial importance to psychopharmacological research. Reports of pharmacological agents which reputedly facilitate learning or retention frequently arise from experiments in which electric shock is used as a motivating stimulus. In many of these initial reports active avoidance was the task which was employed. Several investigators have suggested that the mechanism by which these agents appear to have facilitative effects upon learning is that the agents disrupt "freezing" responses which are usually obtained to electric grid-shock under normal conditions. This hypothesis says that the agent ostensibly facilitates learning only because it "activates" the drugged animal so that it does not "freeze"--a response which is incompatible with performing the active avoidance response--and the animal, therefore, appears to learn faster only because the control animal is retarded in learning because of its freezing behavior. As attractive as this hypothesis has been, and there are several reports of evidence in indirect support of the disruption-of-freezing hypothesis, it has never been put to an adequate, direct test. We feel that a direct test can be made by comparing the effects of a given agent (be it strychnine, picrotoxin, magnesium pemoline, U-9189 or even amphetamine) upon shuttle avoidance learning under a shock UCS with the agent's effect under an air-blast UCS. Freezing does not occur under air-blast conditions in the first place because the escape response is so universally and consistently rapid and well organized (in sharp constast to the extremely variable latency and chaotic nature of the escape response to electric grid-shock) and in the second place because freezing is never reinforced with air-blast, as it is with shock. That is, by freezing, gripping the bars tightly, the animal increases the body surface exposed to the shock

thereby decreasing the current density at any single locus, which, in turn, presumably decreases the noxiousness of the shock. We are very enthusiastic and optimistic about this line of research, and we intend to be generating the necessary data during the coming contract year.

(It should be added parenthetically at this point that one of our auxiliary experiments along this line of interest showed that the reported facilitative effect of magnesium pemoline upon retention was caused by an artifact in the design of Plotnikoff's original experiment, and we also presented indirect evidence in support of a freezing interpretation of the reported facilitative effect upon acquisition of an active jump-out avoidance response. The report is published in Science, 1967, 155, 1281-1282.)

In the process of solving our experimental problems associated with the Vigilance program, therefore, we have evidently stumbled upon a phenomenon of even greater and possibly more wide-spread interest to the scientific community, both in the Edgewood Arsenal Laboratories and perhaps even outside of their direct interests. I would like to take this opportunity to acknowledge the support and research flexibility provided by the present series of research contracts, and to point out the facilitatory effects which such arrangements have had upon unforeseen scientific progress. It is my opinion--and surely only mine at the moment--that this one rather simple yet powerful methodological development, which coincidentally was precisely one of the main goals of this research contract, will alone prove to be worth the support awarded.

The impact, which air-blast UCS will have upon the Vigilance program, has yet to be evaluated. We have constructed a large shuttle box for the Vigilance situation (i.e., an apparatus with one transparent side wall through which the monkey can view the display), and we have begun an experiment designed to compare the relative effectiveness of shock versus air-blast UCS in leading to the visual signal-from-noise detection behavior we need for Vigilance experiments. This work will also continue during the coming contract year.

Visual Exploration

Our progress in this research program can be characterized as having been steady, productive but undistinguished. Early in the contract period, the apparatus used in this program was automated by recording door-opening responses directly onto IBM cards with an on-line, IBM 526 Printing Summary Punch (keypunch). Collation, tabulation and analyses of the data are performed subsequently with the CDC 1604-3600 computer system on this campus.

Most of our work in this program has been to determine the effects of three doses of several drugs upon monkeys' visual exploration behavior. We present our data from these experiments in terms of seven measures: (1) total hourly response frequency as a function of the 10 hours of a recording session, (2) total hourly response duration as a function of 10 hours, (3) average duration per response for each of the 10 hours, (4) total frequency of 21 categories of response duration (0 to 1 minutes, 1 to 2, 2 to 3,...19 to 20, and 20 and greater) over the entire 10-hour session, (5) total duration of

responses within each of the same 21 categories of response duration, (6) total frequency of 21 categories (0 to 1 minute, 1 to 2,...20 and greater) of inter-response duration (duration of no responding), and (7) total duration of no responding accumulated in each of the same 21, inter-response durations.

The following doses and drugs were tested: 0.05, 0.10, and 0.20 mg/kg atropine sulphate; 1.25, 2.50, and 5.00 mg/kg chlorpromazine hydrochloride; 0.125, 0.25 and 0.50 mg/kg d-amphetamine; 1.25, 2.50 and 5.0 mg/kg chlordiazepoxide. The data from all these compounds have been analyzed (each of 12 monkeys received each dose of each drug), and the significant results may be summarized, at least in bold outline, as follows: all doses of atropine rather uniformly depressed response frequency for 7 hours and the highest dose (0.20 mg/kg) reliably increased response duration between the third and the seventh hours. The two highest doses of chlorpromazine (2.5 and 5.0 mg/kg) depressed response frequency for 9 hours, and all doses depressed response duration for 9 hours. The two lowest doses of amphetamine increased response frequency for 8 hours at the 0.25 mg/kg dose and for 3 hours at the 0.125 mg/kg dose. All three doses increased response duration, magnitude and duration of effect being directly proportional to dose; 0.125 mg/kg for 2 hours, 0.25 mg/kg for 6 hours and 0.5 for 9 hours. Chlordiapoxide had no significant effects on any measure. As soon as other compounds are received from Edgewood Arsenal, they will be tested.

Wisconsin Automatic Testing Apparatus

During this contract period, the principal summary report of this program was published (*Perception and Psychophysics*, 1966, 1 405-411). In it we summarized over 2 years of research on the identification of the physical stimulus dimensions which monkeys use in discriminating between two visual metric patterns.

Subsequent to this research, we have added a system for recording response latency (between a mask response and the discriminative response), in addition to the system for recording the discriminative response itself. Since this apparatus modification was effected, we have been occupied with gathering data on two general problems. (1) Using our standard battery of 12 extensively test-sophisticated monkeys, we have been determining the relation between these two dependent measures--response correctness and response latency--in terms of asymptotic learning set performance as a function of the discriminative difficulty of the problem (the pair of stimuli presented). These data are for the most part obtained, and our analyses of them are nearly complete. (2) With a new group of 14 experimentally naive monkeys we are determining (a) the course of learning set development as a function of problem difficulty (e.g., does learning set develop equally rapidly to easy and difficult discriminations or will learning set develop to easier problems first and subsequently generalize to more difficult ones?); (b) the course of development of learning set as indexed by response latency; and (c) again, the relation between response correctness and latency across trials within a given problem and across stages of learning set development. These animals have currently received about 50 problems (25 trials per problem), and we expect the experiment will last throughout the coming contract year.

References

Polidora, V. J. and Boyer, W. N. Avoidance learning by squirrel monkeys: Measures and motivators, Psychon. Sci., 1967, 7, 175-176.

Frey, P. W. and Polidora, V. J. Magnesium Pemoline: Effect on avoidance condiconditioning in rats, Science, 1967, 155, 1281-1282.

Polidora, V. J. Stimulus correlates of visual pattern discrimination by monkeys: Multidimensional analyses, Percept. & Psychophysics, 1966, 1, 405-414.

AD-816682

Security Classification

DOCUMENT CONTROL DATA - R&D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classifi...

1. ORIGINATING ACTIVITY (Corporate author) UNIVERSITY OF WISCONSIN Madison, Wisconsin 53706	2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED 2b. GROUP N/A

3. REPORT TITLE

(6) METHODS FOR MEASURING CHEMICALLY INDUCED BEHAVIORAL CHANGES IN VARIOUS MAMMALIAN SPECIES.

4. DESCRIPTIVE NOTES (Type of report and inclusive dates)

(9) Final Rep[redacted]t. [redacted] Apr[redacted] 65-Dec[redacted] 66.

5. AUTHOR(S) (Last name, first name, initial)

(10) [redacted] Vincent J. Polidora

6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
(11) 15 Dec[redacted] 66	(12) 18p.	3

8a. CONTRACT OR GRANT NO. (15) DA-18-035-AMC-368(A) b. PROJECT NO. (16) DA -1C014501B71A c. d.	9a. ORIGINATOR'S REPORT NUMBER(S) FR 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report) N/A

10. AVAILABILITY/LIMITATION NOTICES

This document is subject to special export controls and each transmittal to foreign governments or foreign nationals may be made only with prior approval of the CO, Edgewood Arsenal, ATTN:SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010

11. SUPPLEMENTARY NOTES Basic research in life sciences	12. SPONSORING MILITARY ACTIVITY Edgewood Arsenal Research Laboratories Edgewood Arsenal, Maryland 21010

13. ABSTRACT

Progress during the 18-month period of this research contract is described in terms of the four principal research programs pursued: (1) Sequential responses (both monkeys and rats), (2) Vigilance, (3) Visual Exploration, and (4) Wisconsin Automatic Testing Apparatus (WATA). The most important advances in each of the programs are as follows. The monkey sequential responses research has been discontinued during the contract period because of inability to train monkeys to execute these response patterns. The rat sequential responses program has continued with the major emphasis being upon experiments on the effects of electrolytic lesions to several subcortical areas of the brain, and the effects of certain hallucinogenic agents both before and after the brain lesion. The single most important outcome of our research during the contract period has been in an outgrowth of the Vigilance program; namely, the experimental advantages of using an air-blast to motivate monkeys (and rats) in shuttle-box avoidance learning and performance. ~~We~~ It was found that an air-blast unconditioned stimulus (UCS) led to more stable and more rapid learning in squirrel and rhesus monkeys, than did an electric grid shock UCS, and similar effects, including an absence of "freezing behavior," was obtained with rats. The balance of the Vigilance research was devoted to drug experiments on visual signal-from-noise detection behavior. The Visual Exploration program was devoted to determining the effects of atropine, chlorpromazine amphetamine and chlordiazepoxide, each tested at three doses and for 10 hours. In the WATA program we have completed our experiments characterizing the stimulus correlates of visual metric pattern discriminability for learning-set sophisticated monkeys, and we have begun our next series of experiments on naive monkeys.

DD FORM 1 JAN 64 1473

UNCLASSIFIED

Security Classification

380 100

elk

Security Classification

14. KEY WORDS		LINK A ROLE	LINK A WT	LINK B ROLE	LINK B WT	LINK C ROLE	LINK C WT
CS	Chlordiazepoxide						
LSD	Receptacle-touch response						
Rats	Cylindrical response patterns						
Monkey	Sequential response patterns						
Vigilance	Psychological characterization effects						
Atropine	Psychopharmacological effects						
Illuminance	Chlorpromazine hydrochloride						
Response rates							
Behavioral changes							
Visual exploration							
Sequence Complexity							
Avoidance behavior							
Mammalian species							
Correct Site Changes							
d-amphetamine							

INSTRUCTIONS

1. ORIGINATING ACTIVITY: Enter the name and address of the contractor, subcontractor, grantee, Department of Defense activity or other organization *(corporate author)* issuing the report.

2a. REPORT SECURITY CLASSIFICATION: Enter the overall security classification of the report. Indicate whether "Restricted Data" is included. Marking is to be in accordance with appropriate security regulations.

2b. GROUP: Automatic downgrading is specified in DoD Directive 5200.10 and Armed Forces Industrial Manual. Enter the group number. Also, when applicable, show that optional markings have been used for Group 3 and Group 4 as authorized.

3. REPORT TITLE: Enter the complete report title in all capital letters. Titles in all cases should be unclassified. If a meaningful title cannot be selected without classification, show title classification in all capitals in parenthesis immediately following the title.

4. DESCRIPTIVE NOTES: If appropriate, enter the type of report, e.g., interim, progress, summary, annual, or final. Give the inclusive dates when a specific reporting period is covered.

5. AUTHOR(S): Enter the name(s) of author(s) as shown on or in the report. Enter last name, first name, middle initial. If military, show rank and branch of service. The name of the principal author is an absolute minimum requirement.

6. REPORT DATE: Enter the date of the report as day, month, year, or month, year. If more than one date appears on the report, use date of publication.

7a. TOTAL NUMBER OF PAGES: The total page count should follow normal pagination procedures, i.e., enter the number of pages containing information.

7b. NUMBER OF REFERENCES: Enter the total number of references cited in the report.

8a. CONTRACT OR GRANT NUMBER: If appropriate, enter the applicable number of the contract or grant under which the report was written.

8b, 8c, & 8d. PROJECT NUMBER: Enter the appropriate military department identification, such as project number, subproject number, system numbers, task number, etc.

9a. ORIGINATOR'S REPORT NUMBER(S): Enter the official report number by which the document will be identified and controlled by the originating activity. This number must be unique to this report.

9b. OTHER REPORT NUMBER(S): If the report has been assigned any other report numbers *(either by the originator or by the sponsor)*, also enter this number(s).

10. AVAILABILITY/LIMITATION NOTICES: Enter any limitations on further dissemination of the report, other than those imposed by security classification, using standard statements such as:

(1) "Qualified requesters may obtain copies of this report from DDC."

(2) "Foreign announcement and dissemination of this report by DDC is not authorized."

(3) "U. S. Government agencies may obtain copies of this report directly from DDC. Other qualified DDC users shall request through ________________."

(4) "U. S. military agencies may obtain copies of this report directly from DDC. Other qualified users shall request through ________________."

(5) "All distribution of this report is controlled. Qualified DDC users shall request through ________________."

If the report has been furnished to the Office of Technical Services, Department of Commerce, for sale to the public, indicate this fact and enter the price, if known.

11. SUPPLEMENTARY NOTES: Use for additional explanatory notes.

12. SPONSORING MILITARY ACTIVITY: Enter the name of the departmental project office or laboratory sponsoring *(paying for)* the research and development. Include address.

13. ABSTRACT: Enter an abstract giving a brief and factual summary of the document indicative of the report, even though it may also appear elsewhere in the body of the technical report. If additional space is required, a continuation sheet shall be attached.

It is highly desirable that the abstract of classified reports be unclassified. Each paragraph of the abstract shall end with an indication of the military security classification of the information in the paragraph, represented as *(TS)*, *(S)*, *(C)*, or *(U)*.

There is no limitation on the length of the abstract. However, the suggested length is from 150 to 225 words.

14. KEY WORDS: Key words are technically meaningful terms or short phrases that characterize a report and may be used as index entries for cataloging the report. Key words must be selected so that no security classification is required. Identifiers, such as equipment model designation, trade name, military project code name, geographic location, may be used as key words but will be followed by an indication of technical context. The assignment of links, rules, and weights is optional.

UNCLASSIFIED
Security Classification